



## Cerebral Infarctions in New-borns and Infants: Early Detection of Risk Factors, and Sequelae in Neuroevolutionary Development

Rufo Campos Miguel<sup>1\*</sup>, Rufo Muñoz Miguel<sup>2</sup> and Rufo Tejeiro Olga<sup>3</sup>

<sup>1</sup>Head of the Child Neurology Service. Instituto Hispalense de Pediatría, Seville

<sup>2</sup>Andalusian Emergency Service, San Isidoro University Center, Seville

<sup>3</sup>Intensive Care Unit, Virgen del Rocío University Hospital, Seville

\*Corresponding Author: Rufo Campos Miguel, Head of the Child Neurology Service. Instituto Hispalense de Pediatría, Seville.

Received: March 01, 2022

Published: March 11, 2022

© All rights are reserved by Rufo Campos Miguel, et al.

### Abstract

Despite the importance of neonatal infarctions, there are very few relative data in our country, both on their frequency, mortality, major risk factors, as well as their important sequelae. In addition, both its pathophysiology and the associated risk factors are not yet clearly understood and defined. Therefore, we tried to establish the percentages of risk, mortality and sequelae of all neonatal strokes that occurred in a large third-level hospital, especially the risk factors that produce it, to try to predict their recurrence.

During a period of 4 years, 53 cases have been collected in which the existence of a recent ischemic-hemorrhagic infarction that occurred during the perinatal period has been demonstrated by neuroimaging a study, making a cut at 30 months of age. Half of the cases were diagnosed within the first month of birth.

The predominance was male and the distribution of cerebral ischemic injury was predominantly of the medial cerebral artery and most often in the left cerebral hemisphere Risk factors were primiparity, fetal death, neonatal sepsis, asphyxia, twin pregnancy, placental abruption, emergency caesarean section, Apgar score  $\leq 7$  after 5 min, breech presentation and hyperbilirubinemia. The guiding sign to start the etiological search was the existence of a motor deficit and the presence of epileptic seizures. In much lower proportions psychomotor retardation.

**Keywords:** Cerebral; Risk Factors; Neuroevolutionary; Sequelae

### Introduction

The publications that are produced on cerebrovascular disease in childhood are show that the guidelines of research and action are based, preferably, on individual clinical experiences, being very few updated protocols. The terms cerebral vascular accident and cerebral infarction are often referred to as a common process, but nevertheless the implicit meaning is that cerebral vascular accident is something that exists at the beginning of the process, when reversibility is still possible, while the expression infarction is used to refer to an irreversible process. One of the clearest definitions of cerebral vascular accident is referred to in the Dorland's Illustrated Medical Dicionary [1] which describes it as "the sudden development of a neurological deficit resulting either from occlusion or from the rupture of a cerebral vessel". On the other hand, infarction is described as the "death of brain or retinal cells due to prolonged ischemia." This definition categorizes both pannecrosis and neuronal death [2].

Stroke is known as a process that causes significant morbidity and mortality in adults, but it is also known in younger patients, and more often in the newborn and during early childhood. This recently led to the Scientific Statements Oversight Committee of the Association's Stroke Council. from the American Heart Association and the Manuscript Oversight Committee of the American Heart Association to create a statement reflecting the experience of published clinical and epidemiological studies, morbidity and mortality reports, clinical guidelines etc. to summarize existing evidence and indicate gaps in current knowledge [3]. These same authors recognize that newborns have the highest risk rate: 1 in 4000 live births will suffer a stroke, well above the rest of the pediatric ages. The word infarction is usually applied to necrotic injury that occurs after the occlusion of an artery, and usually describes tissue responses that extend from coagulation necrosis in a relatively early period after occlusion, to complete cavitation when the lesion

has become chronic. For this reason, when the brain has cavitated, and although it is automatically assumed that the injury has been caused by an arterial occlusion, the truth is that the cause of this is practically impossible to establish [4]. It is necessary to know that, in childhood, cases of infarctions recurrent in almost 20%, but recurrence after a perinatal infarction is exceptional [5].

There are very few data on neonatal infarctions in our country, both on the frequency in large hospitals, and on the percentage of risk factors after the existence of arterial ischemic strokes in the neonatal period. All this moved us to try to establish those percentages within a large population in a third-level hospital, especially those risk factors that also produce it, could predict recurrence.

### Paediatric population studied

The children studied come from the External Consultations of Child Neurology of the Virgen del Rocío University Hospitals in Seville, obtained from the follow-up reviews of all children at neurological risk admitted to the Neonatology Service of the Hospital. During a period of 4 years, all cases of patients have been collected in which, due to various circumstances, a lesion compatible with a recent ischemic-hemorrhagic infarction has been detected on a skull MRI, which has usually produced a neurological disability. As inclusion criteria, it has been necessary to collect in all patients, the existence of an ischemic infarction (including arterial ischemic stroke and thrombosis of the dural sinuses) or hemorrhagic, occurred during the perinatal period, understood this from 20 weeks of gestation to 28 days of life. A cut of 30 months of life has been made as a limit to make its inclusion in the study, and the diagnosis of infarction has necessarily had to be verified by means of an MRI performed during the first 30 months, and reported as positive by a child neuroradiologist of the hospital.

A total of 57 cases have been collected, of which 4 of them have been discarded for not complying with the inclusion criteria described above. One of them for having made the diagnosis outside the hospital and not having the neuroradiological verification, two for having made the diagnosis by MRI later than 30 months of life, and a last case for not having clearly defined the existence of a heart attack that occurred in the neonatal period. To proceed with the statistical study, a total of 35 variables were collected, and for the analysis of the results the SPSS-Version 17 was used, using for the analysis of the data the Chi square the qualitative variables, sometimes performing the correction of Yates. In the event that the qualitative variable had more than two categories, an analysis of variance would be used. The Student-Fisher Test for quantitative

variables. Line or regression equation, to check the degree of participation they have in the variable that we want to predict other variables. And the Pearson Correlation that is applied to check how two quantitative variables co-vary.

### Results

Of the total of 53 cases, 36 of them correspond to men, and 17 cases to women. The age of the entire casuistry at the time of diagnosis was in a range ranging from 0 (newborn) to 29 months of extrauterine life. Weeks of gestation ranged from 26 to 42 weeks. Most of the children were born at term, with an average of 3,046.47 gr., with a minimum of 750 grams and a maximum of 4,180.00 gr, although with a standard deviation of 726.811. In the Apgar tests obtained at 1-5-10 minutes, there was no significant deviation in relation to low Apgar scores.

In 28 cases, no gestational history was collected, and in 5 cases more than one was collected. The most important cause of gestational history was maternal bleeding, 11 cases, followed by 4 cases of infections. Other less frequent causes were drug addiction, (2 cases), the presence of thalassemia in several members of the family, a pregnant woman affected by mitral valve disease, the presence of a possible maternal toxoplasmosis that could not be corroborated, a megakaryocytic thrombopenia in two aunts of the mother and in a maternal first cousin in an RN affected by a megakaryocytic thrombopenic purpura by a passive transfer of maternal antigens, an unspecified polyglobulia in the entire paternal family, the ecetus of a maternal aunt at 40 days of life by a cerebral embolism and mother with a mutation of the gene of prothrombin with a deficit of free protein S and TA III, a mother diagnosed and treated with gestational lues, another of hypertension, and another of absence crisis treated with valproic acid.

Among the family history, the most frequent cause was epileptic seizures and hematological history, followed by vascular malformations, and other types of causes on four occasions.

As for the type of delivery, it was eutocic on 28 occasions, dystocic on six, and a cesarean section was necessary in 19 patients, which represents 35.44% of the casuistry, an abnormally high figure, and that in most cases was related to the presence of meconium (10 cases) or loss of fetal well-being, something that occurred in 7 patients. In one case, the mother suffered a cardiorespiratory arrest during the expulsive period, which forced an urgent cesarean section.

During the newborn period, in 18 cases, no type of pathology was observed. In 25 the patient's poor general condition was observed, which required his immediate admission, In 8 cases a cyanosis appeared, and in one case the presence of hypoxia and an undetermined pathology. In 19 cases, some other type of pathology associated with the one existing in the previous section was presented, and two patients suffered a third associated pathology.

In 33 cases, no personal history appeared that could be of interest, and even less that was related to the possibility of developing a cerebral infarction. Of the rest of the sample, 7 cases had presented critical epileptic manifestations, in 4 cases infections had been detected and in 3, a psychomotor delay. In only two cases, the children were diagnosed with motor deficits, and only one case had the child suffered from dehydration. Finally, another 3 patients would have suffered several processes, such as neonatal meningitis due to intrauterine sepsis due to beta agalactie streptococcus, another with severe post-infectious anemia after another streptococcal meningitis, and another patient who after a cerebral hemorrhage made a hydrocephalus, with a ventricular infection, need for a bypass valve, a retinopathy of prematurity, and finally the emergence of complex partial seizures. One patient was Down syndrome.

Up to 11 patients discovered heart disease during the neonatal period, although some of them were limited to the presence of permeable ductus. Only 5 patients had suffered from serious cardiac pathology: a valvular aortic stenosis that had to be operated on by implanting a balloon 1 mitral insufficiency with dilation of the left cavities that produced a pericardial effusion, and a dilated cardiomyopathy; Another patient diagnosed with Down syndrome, suffered from a complete form of atrioventricular canal, accompanied by a ventricular septal defect and mitral regurgitation; another child was diagnosed with transposition of the large vessels, with a moderate suprapulmonary stenosis, being operated, although he had suffered the infarction prior to the intervention. The last patient was diagnosed with hypoplastic left heart, mitral atresia with permeable aorta, ventricular septal defect, hypoplasia of the aortic arch, and critical coarctation. The rest of the 11 patients with cardiac anomaly were diagnosed with permeable ductus, foramen ovale, and ductus arteriosus. A catheterization was performed on 3 occasions, and there was a need for extracorporeal circulation in one case, having to perform cardiac surgery in four cases.

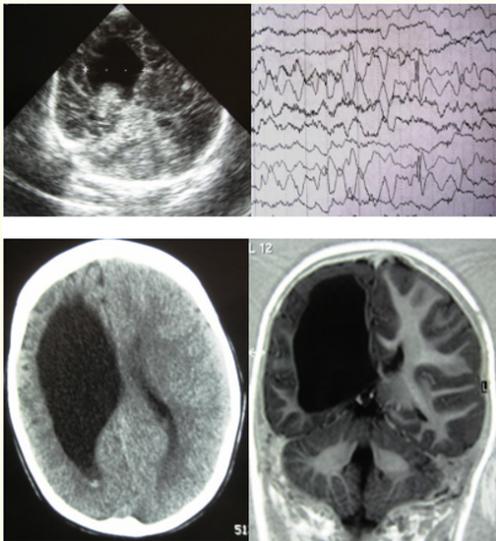
In the assessment of psychomotor development at the time of revision to the Child Neurology consultations, 28 patients did not show any developmental alteration, although a medium delay was

already observed in 15 patients, and a slight psychomotor delay in 9 cases. A single case showed profound psychomotor retardation. In the evolutionary controls of psychomotor development, in 28 cases they were normal and only 12 cases were altered.

The area of development that most affected was the motor area with 34 cases, followed by the cognitive area with 14 cases. On only one occasion was the language altered. Two predominant guide signs were observed: motor deficits (monoparesis, hemiparesis and tetraparesis), with 21 cases followed by epileptic seizures (focal, secondarily generalized and epileptic syndromes) with 20 cases. Psychomotor delay has already remained in eight cases. As guiding signs, hemiparesis among motor deficits (19 cases) and focal seizures among epilepsies (16 cases) were predominant.

In all cases, a conventional biochemistry and an antiphospholipid antibody study were performed. In addition, various factors considered hereditary were investigated and certain genetic studies, such as fetal hemoglobin, or high hematocrit levels or an increase in viscosity, were looked at specifically. Alterations were found in 14 patients, being significant in two of them: one with a deficit of proteins C and S, whose factor V of Leiden did not mutate, detecting a heterozygous mutation of the gene that encodes homocysteine (he was diagnosed with a congenital megakaryocytic thrombopenia and a hypercoagulability syndrome). And another patient with a slight deficit of AT-III and protein S, being diagnosed with congenital thrombophilia by heterozygous mutation G20210A of the prothrombin gene. The other alterations were an alteration of the RPCa with a long TTPA, a transient thrombopenia, a slight increase in fibrinogen, a discrete increase in lupus anticoagulant, alterations of the QUICK and the TPTA with an overall decrease in coagulation except factor VIII, a hemorrhagic disease of the RN, several selective increases in C-reactive proteins and S protein, isolated platelets, positivity of anticardiolipin Ig antibodies that needed to be treated with acenocoumarol, and a selective disorder of iron metabolism.

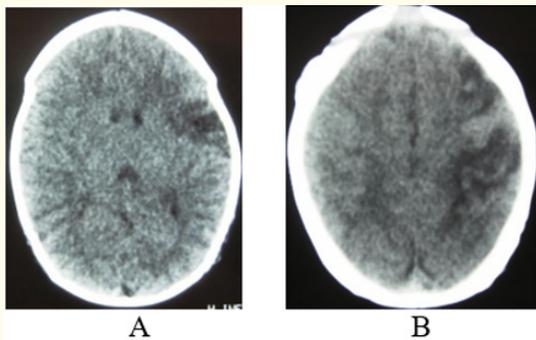
Neuroimaging studies (Figures 1 and 2) have been the pillar on which all the work has been based. When the frequency tables of the results of the transfontanelar brain ultrasound were analyzed in 26 cases, it was not considered as a necessary element for the etiological investigation of the child and did not provide any data of interest in 12 cases of the 27 in which it was carried out. In the rest, if anomalies were found that justified its realization.



**Figure 1:** Clinical case G.P.L.

A male of 2 years and 1 month of age, with no history of interest, who in a prenatal ultrasound detects a dilation of the VLD. A few days after birth, episodes of partial seizures begin. The biochemistry and the rest of the study show no abnormalities, and in the neuroimaging a right prenatal hemorrhagic infarction is observed.

Confirmive ultrasound, EEG, CT and MRI of the case.



**Figure 2:** Clinical case J.Z.M.

A 4-year-old male, diagnosed with RN of complex heart disease, in which a stroke is detected prior to the intervention of his heart disease.

Cranial CT: A) Ischemic infarction in acute phase, left sylvian, diverting midline structures, in the distribution territory of the middle cerebral artery. B) Same patient at 7 days. In coronal cuts, hyperdense images appear on the lesion that lead to thinking of bleeding.

The cranial CT scan was performed in 41 cases, not having been considered necessary in 12 of them. In 37 cases they were considered positive when images compatible with ischemic or hemorrhagic infarctions were detected; in 4 children it was considered normal, but the infarction was later appreciated in the resonance images. In 40 cases, an MRI of the skull was performed for diagnostic confirmation as the general condition of the patient allowed, after the performance of other neuroimaging studies. Cerebral angiographic studies have been performed only in 5 patients, having performed 3 angio-MRI and only 2 conventional angiographies. Regarding the characteristics of the brain injury caused by the infarction, in 33 cases they were classified as medium; small-sized lesions with 13 cases and large-sized ones, 7 cases. The type of lesion was considered ischemic in 46 cases, and in 7 cases hemorrhagic. In most cases, several lesions had occurred, so the location was multiple in 18 patients, followed by a location in the parietal lobe in 16 cases. In the temporal and frontal regions the lesions settled in two cases each, and in a single case the lesion was located in the occipital region. Lateralization of the lesion occurred in the left hemisphere on 24 occasions and in 20 cases in the right hemisphere. In 7 patients, the location was clearly bilateral.

Two patients resorted to the production of the infarction. One of them, diagnosed at 5 months of age, without a family or gestational history of interest, had to be readmitted for intense cyanosis, and in the cardiological study, a complex heart disease was detected, with a hypoplastic left heart, with atresia of the mitral valve and permeable aortic valve, C.I.V., hypoplasia of the aortic arch and critical coarctation. In successive controls, two new areas of infarction are detected, which cast a shadow over the prognosis. A second infant, with no family or gestational history of interest, was first diagnosed at 11 months of age, when hemiparesis was detected in a routine well-child check-up. In the neuroimaging tests, several small infarctions could be visualized, located in the thalamus, temporal lobe, cerebellum and corpus callosum. A significant elevation of lupus anticoagulant was detected, and he suffered new ischemic infarctions. The neurological examination was altered in 39 cases and almost all corresponded to motor deficits. On one occasion, a sensory deficit was detected that later developed into West syndrome, profound psychomotor retardation, and spastic tetraparesis; Neuroimaging studies revealed a bilateral ischemic lesion located in the thalamus and basal ganglia, and agenesis of the corpus callosum.

## Discussion

With a prevalence of one per-2,300-5,000 births, [6] perinatal cerebral infarction is the most frequent form of stroke (CVA) in childhood, despite the fact that half of the cases go unnoticed during the perinatal period, and are usually diagnosed months or even years later, with the presence of a motor brain disease, an epileptic seizure, a cognitive deficit or fortuitously in a radiological examination. In the rest, the clinical presentation is early, usually with repeated and isolated partial seizures in the first three days of life. And it is by performing a neuroimaging study when the diagnosis is confirmed, by discovering ischemic lesions limited to an arterial territory. It is estimated that they currently affect about 5 million people worldwide. [7] Their importance lies in the fact that they constitute one of the 10 most frequent causes of mortality in childhood [8]. In our hospital, out of a total of 8,042 admissions over a period of four years, we collected 53 cases, representing an incidence of 0.65% of the total number of patients admitted during that period in the Neonatology Service. Strokes occur throughout life, but the age distribution shows two large peaks of incidence: the fetal-neonatal period and those over 45 years, in both cases, these are infarctions, hemorrhages, and venous thrombosis with or without associated infarction. The high incidence in the male sex in our series is striking, but this is common when consulting other studies with a high number of cases [9]. The greatest diagnostic difficulty occurs in those patients with epileptic seizures who have suffered a hypoxo-ischemic encephalopathy.

Outside the context of acute neonatal encephalopathy due to asphyxiation, this type of infarction takes place mainly in full-term newborns, mostly children of primiparous mothers, product of a birth usually anodyne, but who debut with seizures and involvement of the general state within a few hours or days of extrauterine life. The affectation of a clear vascular territory predominates in them, unlike cases of asphyxia in which the diffuse disorder affects multiple territories in a heterogeneous way, and different also from cases with less severe asphyxia, in which parasagittal lesions are frequently associated.

The factors most involved in its pathogenesis are placental embolization due to degeneration of this or maternal autoimmune disease, obstetric trauma, maternal cocaine intake, intravascular catheterization and states of hypercoagulability. The healthy term

newborn is characterized by a series of hematological factors that define it as hypercoagulable in comparison with older children and adults. Prothrombotic factors are most abundant (factors V and VIII, fibrinogen and platelets) during the neonatal period, while antiplatelet forces are depressed and show some maturation delay (antithrombin III and protein C). Situations such as labor stress, trauma, infections, and toxins can easily destabilize this precarious balance [10]. In addition, numerous studies on genetic factors for prothrombotic risk have appeared in recent years. Its prevalence in children of any age with cerebral infarction is much higher than that of the normal child population, whether here are associated structural factors potentially causing the injury. This occurs in a quarter of cardiopaths with cerebral ischemic infarction during childhood [11].

Since the last works of G. Kenet [10], the importance of thrombophilia as a risk factor in the production of infarctions in neonatal patients has been demonstrated. Other hematological alterations such as those found in this series are sufficiently verified [12-14] highlighting all these studies that the prothrombotic genetic risk factors, play a very important role in the triggering of symptomatic ischemic infarctions, being shown that a hematological factor of prothrombotic risk is present in more than 40% of patients, and up to 30% suffer more than one of these or another type of factors (stained fluid, heart disease, etc.), which would influence the final outcome of the process, and in some cases there may be a concurrence of conditions that are not entirely optimal at the time of delivery, all of them contributing to the final outcome [15].

When we tried to relate the different Apgar tests obtained at the 1st, 5th, and 10th with the fact of suffering or not ischemic pathology, it could be objectified that there is no significant deviation in relation to low scores of the Apgar test, so it lacks a clear statistical significance. Among the studies in which family history has been considered, the importance of genetic factors as a risk of suffering a cerebral infarction is gaining strength [3]. While certain genes, such as those predisposing to cerebral ischemia, may increase the risk of ischemic stroke in all major subtypes, other genetic factors such as carotid atherosclerosis or microangiopathy may be relatively more important in certain etiological subtypes. An example of this is seen in the monogenic disorder of CADASIL disease in which the notch of mutation 3 predisposes specifically for lacunar

infarction. In the present series, the most frequent cause among the antecedents turned out to be epileptic seizures and hematological history, followed by vascular malformations, and other types of causes on four occasions. In one case, more than one family history was detected and in another, up to three relatives with a history, possibly related to the ischemic process.

Among the perinatal factors identified, maternal primiparity, infertility, cocaine use, prothrombotic disorders, early rupture of the bursa, abnormal cardiotocography, instrumental deliveries and urgent cesarean sections are frequent causes of the disease. Not surprisingly, the presence of multiple risk factors increases the chances of developing a heart attack. Among preterm infants, they are fetal cardiac abnormalities, twin-to-twin transfusion and hypoglycemia [16,17]. The high number of caesarean sections of the casuistry is striking, but we think that it should be related with the presence of meconium in a significant number of cases, or the loss of fetal well-being, and only as an exceptional case that of a pregnant woman who suffered a cardiac arrest during the expulsive period.

As is known, one of the most important risk factors in the development of all types of infarctions is the existence of any type of cardiac involvement: congenital or acquired heart disease, cardiovascular surgery maneuvers, catheterization, or the existence of acquired heart disease [18] as in this series. And these data are of great importance, since the etiology of neonatal infarctions remains unknown in most cases [19]. It should be borne in mind that neurological complications occur in 25% of cases of non-operated heart disease and, at the same time, a high percentage of children with heart disease have malformations of the central nervous system. And it is known that about half of patients with heart disease will require surgical treatment during the first year of life, with neurological complications being the most frequent [20]. Nor was a clear statistically significant relationship between the presence of complex heart disease as the origin of cerebral infarction and the subsequent presence of epileptic seizures in these same patients found in the present sample.

The area of development that deteriorated the most was the motor area, followed by the cognitive area with 14 cases. On only one occasion was the area most affected by language.

A correct diagnosis of neonatal cerebral infarction is essential for the selection of a treatment and for the prediction of results. When an attempt has been made to look for possible errors in their diagnosis by retrospectively studying the medical histories of 45 patients with cerebral ischemic infarction, and comparing the initial clinical diagnosis with the final etiological diagnosis, up to 24 changes in the diagnosis were identified: 19 initial symptoms that were not attributed to the infarction, and 5 in the change of etiology, forcing to change the treatment in 17 patients [21]. We were able to detect that there are two neurological signs that predominate in these patients: motor deficits (monoparesis, hemiparesis and tetraparesis), which with 21 cases dominates the section of guide signs, followed very closely with the presence of epileptic seizures, with 20 cases. Psychomotor delay is already a long way away, with 8 cases. And hemiparesis predominates among the guide signs, with 19 cases and focal seizures within epileptic semiology with 16 cases. The most specific complementary test for the diagnosis is, by far, the MRI of the skull, something in which all the series consulted agree [22,23], and which we have also verified. In most cases we have not even considered the performance of an ultrasound, and although with less reliability than MRI, the performance of a cranial CT scan was useful to visualize the presence of the infarction. Despite its importance, especially in vascular pathology in adulthood, cerebral angiographic studies were performed on 5 patients: three angio-MRI and two conventional angios.

Skull MRI allowed us to identify subtle ischemic lesions of periventricular white matter, not detected by brain scan or ultrasound. Lesions caused by hypoxia-ischemia, can affect the basal ganglia, grooves of the white matter and the cortex, having shown that the performance of an MRI in the second week of life it can show a much more specific result than the rest of neuroimaging tests, since it is able to detect the ischemic areas of the brain of newborns who have focal or multifocal seizures, infarcted areas that are normally in the perfusion territory of the middle cerebral artery, and most often in the left hemisphere. Always considering the timing of the scan, as it can be negative in the first two or three days after a crisis [24].

With the MRI images, all the characteristics of the brain injury caused by the infarction were studied, both the size, the type of lesion, the location, and by assume the hemisphere in which it is

located. Most of the lesions were classified as medium, followed by small-sized lesions, and those of large size in the fewest cases. The lesion was ischemic in a high percentage of cases, and hemorrhagic in a few. Most of the lesions had a multiple location or located in the parietal lobe, as usual. An essential help in correlating clinical semiology with infarction was to establish lateralization of the lesion: the location was similar in both hemispheres and was scarcely bilateral. As in other important studies involving large patient series [25], only two children relapsed in the production of infarction.

Paediatric heart attacks generally have serious long-term consequences. And, in fact, most survivors show a functional deficit that affects not only their daily lives, but the rest of the child's actions and the life of the family. Our series coincides, with most of the work done in this regard, with the fact that motor sequelae are the most frequent of all the pathology presented by these patients, many of them in the form of cerebral palsy, epilepsies, and cognitive impairment, while a few others have a normal result [26,27].

What is widely demonstrated is that a delay in diagnosis is associated with an increased risk of cerebral palsy, and that there are important relationships between the large size of the infarction, and lesions in the Broca area, internal capsule, Wernicke's area, or basal ganglia, as in the present series [28,29]. However, we have not found any relationship between the lateralization of brain lesions with the different types of delay, nor between the presence of different types of seizures with lateralization or with the size of the lesion. But of course, this relationship exists between the appearance of epileptic seizures, with the development of a psychomotor delay in the subsequent evolution.

The detailed results of epilepsy affecting children in the neonatal period who develop a cerebral infarction, with cognitive or motor impairment have not been well studied. And critical manifestations are very frequent when perinatal infarction takes time to diagnose, and especially when infantile spasms appear at any time. But not everything is negative, and fortunately despite the high incidence of epilepsy in children with hemiplegic cerebral palsy due to a cerebral infarction, the prognosis for epileptic seizures to subside is usually good, and many of these children have clinical, electroencephalography, and remission features typical of idiopathic partial epilepsies [30]. When in the present sample epileptic seizures have been related to the characteristics of brain in-

jury and delay, we have been able to see how there is no statistically significant relationship between the presence of various types of seizures with lateralization or with the size of the lesion. However, the relationship in the appearance of epileptic seizures with the development of psychomotor delay in the subsequent evolution is significant.

In recent years, there has been a tendency to offer multicentric recommendations, both for the initial treatment and especially for the sequelae of those children affected by a perinatal infarction. The main innovations concern the occasional use of anticoagulation in a newborn with venous thrombosis and the re-education of hemiplegia [31].

## Conclusions

Although perinatal cerebral infarction is the most frequent form of stroke in childhood, its diagnosis must be supported by the completion of a neuroimaging study to confirm it. In this series we have found a high incidence in the male sex, being children with a history of epileptic seizures secondary to a neonatal hypoxic picture, which have shown a greater diagnostic difficulty.

No direct relationship has been found between the Apgar test and the production of an ischemic pathology, but with the presence of genetic factors such as the risk of suffering a cerebral infarction. However, we agree with other authors confirming that the greatest risk is the existence of any type of cardiac involvement, especially congenital or acquired heart disease, cardiovascular surgery, or acquired heart disease.

There are several neurological signs that predominate in these patients: motor deficits, psychomotor delay and focal crises. Being the most specific complementary test for diagnosis, MRI of the skull. Early diagnosis is associated with a lower risk of cerebral palsy. It has been shown in our series that there is no significant relationship between the various types of seizures with lateralization or with the size of the lesion, but with neuroevolutionary delay.

## Summary

Despite the importance of neonatal infarctions, there are very few relative data in our country, both on their frequency, mortality, major risk factors, as well as their important sequelae. In addition, both its pathophysiology and the associated risk factors are not yet

clearly understood and defined. Therefore, we tried to establish the percentages of risk, mortality and sequelae of all neonatal strokes that occurred in a large third-level hospital, especially the risk factors that produce it, to try to predict their recurrence.

During a period of 4 years, 53 cases have been collected in which the existence of a recent ischemic-hemorrhagic infarction that occurred during the perinatal period has been demonstrated by neuroimaging a study, making a cut at 30 months of age. Half of the cases were diagnosed within the first month of birth.

The predominance was male, and the distribution of cerebral ischemic injury was predominantly of the medial cerebral artery and most often in the left cerebral hemisphere Risk factors were primiparity, fetal death, neonatal sepsis, asphyxia, twin pregnancy, placental abruption, emergency caesarean section, Apgar score  $\leq 7$  after 5 min, breech presentation and hyperbilirubinemia. The guiding sign to start the etiological search was the existence of a motor deficit and the presence of epileptic seizures. In much lower proportions psychomotor retardation.

### Bibliography

1. Dorland's Illustrated Medical Dictionary, 26<sup>th</sup> Edition. Philadelphia, WB Saunders 1985;101 Jeffrey L Saver. Proposal for a universal definition of cerebral infarction". *Stroke* 39.11 (2008): 3110-3115.
2. Ferriero DM., et al. American Heart Association Stroke Council and Council on Cardiovascular and Stroke Nursing. "Management of Stroke in Neonates and Children: A Scientific Statement from the American Heart Association/American Stroke Association". *Stroke* 50.3 (2019): e51-e96.
3. Radu RA., et al. "Etiologic classification of ischemic stroke: Where do we stand?" *Clinical Neurology and Neurosurgery* (2017): 93-106.
4. Miya E. "Bernson-Leung and Michael J. "Rivkin Stroke in Neonates and Children Pediatrics in Review 37.11 (2016): 463-477.
5. Barnette AR and Inder TE. "Evaluation and management of stroke in the neonate". *Clinics in Perinatology* 36 (2009): 125-136.
6. Mary Dunbar and Adam Kirton. "Perinatal Stroke". *Seminars in Pediatric Neurology* 32 (2019): 100767.
7. Christerson S and Strömberg B. "Childhood stroke in Sweden I: incidence, symptoms, risk factors and short-term outcome". *Acta Paediatric* 99.11 (2010): 1641-1649.
8. Renaud C., et al. "Group. Lipoprotein (a), birth weight and neonatal stroke". *Neonatology* 98.3 (2010): 225-228.
9. Kenet G., et al. "Impact of thrombophilia on risk of arterial ischemic stroke or cerebral sinovenous thrombosis in neonates and children: a systematic review and meta-analysis of observational studies". *Circulation* 121.16 (2010): 1838-1847.
10. Curry CJ., et al. "Risk factors for perinatal arterial stroke: a study of 60 mother-child pairs". *Pediatric Neurology* 37.2 (2007): 99-107.
11. Simchen MJ., et al. "Factor V Leiden and antiphospholipid antibodies in either mothers or infants increase the risk for perinatal arterial ischemic stroke". *Stroke* 40.1 (2009): 65-70.
12. Bernard TJ and Goldenberg NA. "Pediatric arterial ischemic stroke". *Hematology/Oncology Clinics of North America* 24.1 (2010): 167-180
13. Michoulas A., et al. "The role of hypoxia-ischemia in term newborns with arterial stroke". *Pediatric Neurology* 44.4 (2011): 254-258.
14. Mengyu Fan., et al. "Family History, Tobacco Smoking, and Risk of Ischemic Stroke". *Journal of Stroke* 21.2 (2019): 175-183.
15. Cnossen MH., et al. "Paediatric arterial ischaemic stroke: functional outcome and risk factors". *Developmental Medicine and Child Neurology* 52.4 (2010): 394-399.
16. Cheong JL and Cowan FM. "Neonatal arterial ischaemic stroke: obstetric issues". *Seminars in Fetal and Neonatal Medicine* 14.5 (2009): 267-271.
17. Khurana DS., et al. "The role of anticoagulation in idiopathic cerebral venous thrombosis". *Journal of Child Neurology* 11.3 (1996): 248-250.

18. Odland HH, *et al.* "Longitudinal myocardial contribution to peak systolic flow and stroke volume in the neonatal heart". *Pediatric Resesarch* 70.4 (2011): 345-351.
19. Peyvandi S, *et al.* "Neonatal Brain Injury and Timing of Neurodevelopmental Assessment in Patients with Congenital Heart Disease". *Journal of the American College of Cardiology* 71.18 (2018): 1986-1996.
20. Castillo J, *et al.* "Inflammation markers and prediction of post-stroke vascular disease recurrence: the MITICO study". *Journal of Neurology* 256 (2009): 217-224.
21. Counsell SJ, *et al.* "Fetal and neonatal neuroimaging". *Handbook of Clinical Neurology* 162 (2019): 67-103.
22. Hua F, *et al.* "Differential roles of TLR2 and TLR4 in acute focal cerebral ischemia/reperfusion injury in mice". *Brain Research* 1262 (2009): 100-108.
23. Cornette L, *et al.* "Perinatal stroke". *Seminars in Fetal and Neonatal Medicine* 14.5 (2009): 243-244.
24. Caso JR, *et al.* "Toll-like receptor 4 is involved in subacute stress-induced neuroinflammation and in the worsening of experimental stroke". *Stroke* 39 (2008): 1314-1320.
25. Cao CX, *et al.* "Reduced cerebral ischemia-reperfusion injury in Toll-like receptor 4 deficient mice". *Biochemical and Biophysical Research Communications* 353 (2007): 509-514.
26. Urra X, *et al.* "Monocytes are major players in the prognosis and risk of infection after acute stroke". *Stroke* 40 (2009): 1262-1268.
27. Yang QW, *et al.* "Upregulated expression of toll-like receptor 4 in monocytes correlates with severity of acute cerebral infarction". *Journal of Cerebral Blood Flow and Metabolism* 28 (2008): 1588-1596.
28. Kirkham FJ, *et al.* "Risk factors for arterial ischemic stroke in children". *Journal of Child Neurology* 15 (2000): 299-307.
29. Ganesan V, *et al.* "Abnormalities of cervical arteries in children with arterial ischemic stroke". *Neurology* 76.2 (2011): 166-171.
30. Vasudevan C and Levene M. "Epidemiology and aetiology of neonatal seizures". *Seminars in Fetal and Neonatal Medicine* 18.4 (2013): 185-191.
31. Dunbar M and Kirton A. "Perinatal Stroke". *Seminars in Pediatric Neurology* (2019): 32.

#### Assets from publication with us

- Prompt Acknowledgement after receiving the article
- Thorough Double blinded peer review
- Rapid Publication
- Issue of Publication Certificate
- High visibility of your Published work

Website: [www.actascientific.com/](http://www.actascientific.com/)

Submit Article: [www.actascientific.com/submission.php](http://www.actascientific.com/submission.php)

Email us: [editor@actascientific.com](mailto:editor@actascientific.com)

Contact us: +91 9182824667